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Hypoxic-Ischemic Injury in the Term Infant: Clinical-Neurological Features, Diagnosis, Imaging, Prognosis, Therapy

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The clinical aspects of neonatal hypoxic-ischemic encephalopathy (HIE) are appropriately discussed following the neuropathology (see Chapter 18) and pathophysiology (see Chapter 19), because understanding of the clinical phenomena is facilitated greatly by an awareness of the underlying pathological substrates. Moreover, choice of appropriate diagnostic modalities, formulation of rational prognostic statements, and development of appropriate plans of management are based, in many ways, on awareness of the probable neuropathologies. In this chapter, we discuss the clinical settings for neonatal HIE, the clinical syndrome, diagnostic studies, clinical correlations, prognosis, and management.

CLINICAL SETTINGS

The importance of the early recognition of the clinical risk factors for hypoxic-ischemic cerebral injury in the term born infant has escalated significantly in the last decade with the implementation of successful neuroprotection with therapeutic hypothermia (see later sections). To initiate such therapy requires a recognition of the infant who may have suffered hypoxic-ischemic cerebral injury—predominantly in the peripartum period. *The peripartum period is defined as the period shortly before, during, and immediately after birth.* The clinical settings for neonatal HIE are dominated by the ultimate occurrence of ischemia (i.e., diminished blood supply to brain), usually, but not necessarily, preceded or accompanied by hypoxemia (i.e., a diminished amount of oxygen in the blood supply). Hypoxemia leads to brain injury principally by causing myocardial disturbance and loss of cerebrovascular autoregulation, with ischemia the major consequence. The temporal characteristics and the severity of the hypoxemia and ischemia, as well as the gestational age of the infant, are the principal determinants of the type of resulting neuropathology (see Chapters 18 and 19).

The major causes of serious hypoxemia in the peripartum period are: (1) hypoxia-ischemia with intrauterine disturbance of gas exchange across the placenta (i.e., asphyxia) or with failure to establish independent respiration at the time of birth or both; (2) postnatal respiratory insufficiency secondary to severe respiratory disease; and (3) severe right-to-left shunt secondary to persistent fetal circulation or cardiac disease. The major causes of serious ischemia are: (1) intrauterine asphyxia (i.e., hypoxemia, hypercarbia, and acidosis) with cardiac insufficiency and loss of cerebrovascular autoregulation both in utero and at the time of birth; (2) postnatal cardiac insufficiency secondary to severe hypoxemia or congenital heart disease; and (3) postnatal (postcardiac) circulatory insufficiency secondary to patent ductus arteriosus (with "ductal steal") or vascular collapse (e.g., with sepsis).

In this chapter, we will focus on the encephalopathic syndrome in the term infant *and* the presence of evidence for peripartum hypoxic-ischemic injury. We prefer the term "peripartum" hypoxic-ischemic injury as it acknowledges the potential presence of (1) fetal or maternal prepartum conditions that may accentuate propensity to intrapartum hypoxic-ischemic injury; (2) intrapartum hypoxic–ischemic injury per se; and (3) the often associated protracted postpartum resuscitative efforts for such infants, with no or low heart rate for several minutes. Although the postnatal cardiac compromise is not the primary etiology of the poor birth transition, it may contribute to the extent of the ultimate hypoxic-ischemic cerebral injury in the infant. However, there is also evidence that even with prolonged resuscitation, in the era of therapeutic hypothermia there can be better outcomes than might be expected (see the section on prognosis).[1]

It is important to recognize that not all neonatal encephalopathies are related to hypoxic-ischemic disease. Antepartum and postpartum disorders (e.g., infectious, metabolic, dysgenetic) may lead to neonatal encephalopathies,[2,3] as discussed throughout this book. In one large population-based observational study, the prevalence of moderate to severe encephalopathy was 1.64 per 1000 live term births, and the prevalence of "birth asphyxia" was 0.86 per 1000 live term births.[4] Fully 56% of all cases of newborn encephalopathy were related to hypoxic-ischemic injury that occurred during the intrapartum period. These findings are consistent with a more recent large cohort study of 4165 singleton term infants with any one of the following: seizures, stupor, coma, Apgar score at 5 minutes less than 3 and/or receiving hypothermia therapy.[5] In this study, 15% of the infants experienced a clinically recognized sentinel event, such as antenatal hemorrhage (presumably, often placental abruption), uterine rupture, or cord prolapse, all of which are capable of compromising oxygen supply. Almost one half of the infants displayed umbilical cord blood gas acidemia and/or fetal bradycardia. Of note, signs of inflammation were also not uncommon with 27% of mothers displaying elevated maternal temperature in labor and 11% clinical chorioamnionitis. However, the contributing role of chorioamnionitis is not consistently supported.[6] Although intrapartum sentinel events provide clear

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